infection, a bacterial infection, a fungal infection, a cancer, or a foreign peptide fragment in a mammal by inoculating the mammal with two different vectors encoding at least one antigen that is the same.

The Pending Claims

Claims 1-8 are currently pending. Claims 1-8 are directed to the methods.

The Amendments to the Specification and Claims

Page 1, line 3, of the specification has been amended to reflect properly the claim of priority. Furthermore, page 5, line 7, of the specification has been amended to include descriptions for Figures 1A-1E in the "Description of the Drawings." Claims 1 and 5 have been amended to recite a method for inducing an immune response against at least one antigen by inoculating the mammal with two different vectors and, optionally, a nucleic acid encoding an immunostimulatory protein, as supported by the specification at, for example, page 6, lines 27-35, page 7, lines 1-4, and page 8, lines 6-19. Claims 2-4 and 6-8 have been amended to address matters of form. Thus, no new matter has been added through amendment of the specification and claims. Separate documents setting forth the amendments to the specification and claims, as well as the currently pending claims, are enclosed.

The Final Office Action

Claims 1-20 have been rejected under 35 U.S.C. § 112, first and second paragraphs, and under 35 U.S.C. § 103. Reconsideration of these rejections is hereby requested.

Discussion of Rejection under 35 U.S.C. § 112, first paragraph

Claims 1-8 have been rejected under Section 112, first paragraph, as containing subject matter, which allegedly was not described in the specification in such a way as to convey reasonably to one ordinarily skilled in the art that the inventors had possession of the claimed invention. The Office contends that the term "antigen associated disease" is new matter lacking support in the specification. This term has been amended in favor of more specific types of antigens as supported by the specification, at for example, page 11, lines 5-24. Additionally, the Office contends that the phrase "at least one antigen" lacks support in the specification. Applicants disagree inasmuch as the phrase is

supported by the specification at, for example, page 4, lines 22 and 25, page 6, line 35, page 7, lines 3-4 and 17, and page 8, lines 7 and 10-11. In view of the foregoing, Applicants request the withdrawal of this rejection.

Claims 1-20 have been rejected under Section 112, first paragraph, because the specification allegedly does not reasonably provide enablement for obtaining an enhanced immune response using any combination of vectors as broadly claimed or treating cancer as claimed. Claims 9-20 have been canceled in an effort to advance prosecution and not in acquiescence of the rejection. Therefore, the rejection as it pertains to treating cancer is believed to be moot.

With respect to claims 1-8, Applicants respectfully submit that the specification teaches how to make and use the instantly claimed method. The specification teaches at, for example, page 7, line 5 *et seq*, that any recombinant vector can be used in the context of the present inventive method. At page 9 *et seq*, the specification teaches the use of viral vectors in the context of the present inventive method and describes examples of viral vectors suitable for use in the present inventive method. See, also, page 21, for example. Antigens are taught in the specification at, for example, page 11, line 4, *et seq*. Immunostimulatory molecules, other than an antigen of the infectious disease, autoimmune disease, viral infection, bacterial infection, fungal infection, cancer or foreign peptide fragment against which an immune response is to be induced, are described in the specification at, for example, page 13, line 19, *et seq*. Dosages are taught at, for example, page 16, line 6, *et seq*, whereas dosage forms are taught, for example, at page 16, line 31, *et seq*. Routes of administration are taught at, for example, page 17, line 2, *et seq*. In the absence of evidence to the contrary, the Office must accept the specification as enabling. In this regard, Applicants point out that, while the Office continues to maintain that the specification does not enable the use of any combination of vectors, the Office has failed to cite any support for its contention.

While the Office contends that claim 1, *as written*, does not have an enabled use, this issue is believed to be moot in view of the amendments to claim 1. For the record, Applicants adamantly disagree with the Office's characterization of page 4, lines 2-13, of the instant specification as set forth in the final Office Action in the paragraph bridging pages 3 and 4, and direct the Office's attention to page 18, lines 26-33, where enhanced immune responses to influenza nucleoprotein, as well as to β-galactosidase, are reported.

In view of the foregoing, Applicants submit that claims 1-8 are enabled. Accordingly, Applicants request the withdrawal of this rejection.

Discussion of Rejection under 35 U.S.C. § 112, second paragraph

Claims 1-20 (claims 9-20 have been canceled herein) have been rejected under Section 112, second paragraph, as allegedly indefinite for failing to point out particularly and claim distinctly the subject matter of the invention. Applicants respectfully disagree with this rejection. In order to expedite prosecution of this application and not in acquiescence of the rejection, Applicants have amended claim 1. Amended claim 1 clarifies the term "heterologous" to mean two different DNA vectors. Additionally, amended claim 1 substitutes "a second recombinant vector comprising a nucleic acid insert encoding at least one antigen of the infectious disease, autoimmune disease, viral infection, bacterial infection, fungal infection, cancer or foreign peptide fragment against which an immune response is to be induced, wherein the second DNA vector is different from the first DNA vector and wherein at least one antigen encoded by the insert of the first recombinant vector is encoded by the insert of the second recombinant vector" for the rejected phrase "a second DNA vector and the nucleic acid encoding said antigen." Finally, in claim 1, the rejected language "antigen-associate disease" has been replaced with "an antigen of... ." The amendment of claim 1 is also believed to clarify that the induced immune response is towards the encoded antigen(s).

Finally, claim 5 has been amended to recite "protein other than an antigen...," instead of "molecule," as suggested by the Office. In addition, claims 9 and 14 have been cancelled.

In view of the foregoing, Applicants submit that claims 1-8 are definite. Accordingly, Applicants respectfully request withdrawal of the rejection under Section 112, second paragraph.

Discussion of Rejection under 35 U.S.C. § 103

Claims 1-3, 5-7, 9, 14-16, 18 and 19 have been rejected under Section 103 as allegedly obvious in view of and, therefore, unpatentable over Wang (J. Immunol., (1995 May 1) 154 (9): 4685-92). Given that claims 9-20 have been canceled, this rejection will be discussed with respect to claims 1-3 and claims 5-7.

Applicants respectfully submit that claims 1-3 and 5-7 are not obvious in view of Wang since the pre-immunization experiment on page 4689 and Figure 4 of Wang does not teach inducing an effective immunological response by inoculating with different vectors encoding the same antigen, as does the present invention. Rather, Wang teaches pre-immunization with a wild-type viral vector and immunization with a viral vector encoding an antigen. Specifically, Wang states, "[i]nterestingly, mice initially challenged with FPV (fowlpox virus) did not suppress the anti- β-gal response when subsequently challenged with either HPV16-E6Vac (B-gal expressing vaccinia virus) or FPV.bg40k (β-gal expressing fowlpox virus)" (page 4689, col. 2, 1st para.). Thus, it would not have been obvious to one of ordinary skill in the art at the time of the present invention that, in view of Wang, inoculating with a vector encoding at least one antigen followed by inoculating with a different vector encoding at least one antigen, wherein at least one of the antigens encoded by the vectors is the same, would induce an immune response against the antigen. The scope of the present invention is specifically directed to the use of two different vectors encoding antigen(s), at least one of which is the same antigen.

Furthermore, the Office sites Fig. 6 of Wang as showing 50% lysis of β-gal expressing cells that were pre-immunized with wild-type vaccinia virus and then immunized with a recombinant fowlpox virus, and alleges that these data make it obvious to one of ordinary skill in the art to pre-immunize with a recombinant vector followed by immunization with a different recombinant vector expressing the same antigen in order to elicit an immune response. Yet, here again, there is no teaching or suggestion to inoculate in the manner taught by the present invention, i.e., with different recombinant vectors, both of which encode at least one antigen in common so as to induce an immune response against the encoded antigen. Furthermore, with respect to claim 5, the Office admits that "Wang did not expressly teach performing the method wherein the vectors encode an immunostimulatory molecule" (Official Action page 14, lines 13-14). Accordingly, Applicants respectfully request withdrawal of the rejection of claims 1-3 and 5-7 under Section 103.

Claims 1-3, 5-7, 9, 12-16, 18 and 19 have been rejected under Section 103 as allegedly obvious in view of and, therefore, unpatentable over Wang combined with Orlow (1995, PNAS, Vol. 92, pages 10152-10156). Given that claims 9-20 have been canceled, this rejection will be discussed with respect to claims 1-3 and claims 5-7.

Wang does not teach or suggest the subject matter of claims 1-3 and 5-7 for the reasons set forth above. Orlow does not cure the deficiencies of Wang. Orlow merely teaches a new nucleic acid sequences for an antigen, but does not teach or suggest that two different vectors encoding at least one common antigen be used, one after the other, to express TRP-1 or 2 in order to induce an immune response. Accordingly, Applicants respectfully request the withdrawal of this rejection.

Similarly, claims 1-9 and 14-20 have been rejected under Section 103 as allegedly obvious in view of and, therefore, unpatentable over Wang combined with Zhai (Jan. 15, 1996, J. Immunol., Vol. 156, No. 2, pages 700-710). Given that claims 9-20 have been canceled, this rejection will be discussed with respect to claims 1-9.

Wang does not teach or suggest the subject matter of claims 1-8 for the reasons set forth above. Zhai does not cure the deficiencies of Wang. Zhai is directed toward administering an adenoviral vector encoding β-gal. Zhai does not teach inoculating a mammal with a vector encoding at least one antigen followed by inoculating the mammal with a different vector encoding at least one antigen that is the same in order to induce an immune response, as does the present invention. Accordingly, Applicants respectfully request the withdrawal of this rejection.

Conclusion

The application is considered to be in good and proper form for allowance, and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,

Date: November 6, 2002

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In re Appln. of Chamberlain et al.
Application No. 09/838, 987

CERTIFICATE OF MAILING

I hereby certify that this AMENDMENT AND RESPONSE TO FINAL OFFICE ACTION (along with any documents referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner of Patents and Trademarks, Washington, D.C. 20231.

Date: November 6, 2002 Kathleen M. Grant

PATENT
Attorney Docket No. 218654
DHHS Ref. No. E-087-96/2

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Chamberlain et al.

Application No. 09/838,987

Filed: September 6, 2002

Art Unit: 1632

Examiner: Wilson, M.

For: HETEROLOGOUS
BOOSTING IMMUNIZATION

AMENDMENTS TO SPECIFICATION AND CLAIMS IN RESPONSE TO FINAL OFFICE ACTION DATED SEPTEMBER 6, 2002
(Insertions Indicated By Underlining; Deletions Indicated By Brackets)

SPECIFICATION

Page 1, line 3 - This application is a continuation of U.S. patent application no. 09/171,086, filed January 22, 1999, now abandoned, [and] which is the national phase of international patent application no. PCT/US97/06632, filed April 21, 1997, now lapsed, which claims the benefit of U.S. provisional patent application no. 60/015,893, filed April 22, 1996, now lapsed. [09/171,086.]

At page 5, line 7:

Fig. 1: [Shows prolonged survival of tumor-bearing animals after immunizing and boosting with different recombinant vectors.] Compares the effect of repetitive immunization of the recombinant vaccine vectors on tumor growth and long-term survival in BALB/c mice intravenously challenged with 10^5 CT26.CL25 tumor cells to establish pulmonary metastases. The mice were primed with various vectors 3 days post-intravenous challenge and then boosted with same amount and array of vectors 17 days after tumor inoculation. **Fig. 1A** – data of mice primed with no immunogen (None) and later boosted by either no immunogen, 10^7 PFU of rVV expressing β-gal (VJS6), 10^7 PFU of rFPV expressing β-gal (rFPV) or 10μg of pCMV/ β-gal (DNA). **Fig. 1B** – data of mice primed with VJS6 and later boosted by no immunogen, VJS6, rFPV or DNA.

Fig. 1C – data of mice primed with rFPV and later boosted by no immunogen, VJS6, rFPV or DNA. **Fig. 1D** – data of mice primed with DNA and later boosted by no immunogen, VJS6, rFPV or DNA. **Fig. 1E** – data of mice primed with no immunogen, VJS6, rFPV or DNA and then boosted with DNA. The no treatment group (None – None) is shown in all graphs of **Fig. 1** as a control group.

CLAIMS

1. (Thrice Amended) A method for [immunizing a mammal] inducing an immune response against [an] at least one antigen of an infectious disease, an autoimmune disease, a viral infection, a bacterial infection, a fungal infection, a cancer, or a foreign peptide fragment in a mammal, which method comprises: [associated disease inducing an effective immunological response against at least one antigen in the mammal using heterologous boosting immunization by:]

(i) inoculating the mammal with a first recombinant vector comprising a [DNA vector and a] nucleic acid insert encoding at least one antigen of the infectious disease, autoimmune disease, viral infection, bacterial infection, fungal infection, cancer or foreign peptide fragment against which an immune response is to be induced; and

(ii) inoculating the mammal with [a boosting immunization with] a second recombinant vector comprising a [second DNA vector and the] nucleic acid insert encoding [said] at least one antigen of the infectious disease, autoimmune disease, viral infection, bacterial infection, fungal infection, cancer or foreign peptide fragment against which an immune response is to be induced, wherein [said] the second DNA vector is different from [said] the first DNA vector and wherein at least one antigen encoded by the insert of the first recombinant vector is encoded by the insert of the second recombinant vector, [thereby inducing an effective immunological] whereupon an immune response [thereby immunizing] against at least one antigen of the infectious disease, autoimmune disease, viral infection, bacterial infection, fungal infection, cancer or foreign peptide fragment is induced in the mammal [against the antigen].

2. (Twice Amended) The method according to claim 1, wherein the first recombinant vector is [comprises] a recombinant vaccinia [virus] viral vector.

3. (Twice Amended) The method according to claim 1, wherein the first recombinant vector is [comprises] a recombinant fowlpox [virus] viral vector.

4. (Twice Amended) The method according to claim 1, wherein the first recombinant vector is [comprises] a recombinant [adenovirus] adenoviral vector.

5. (Third Amendment) The method according to claim 1, wherein the insert of the recombinant vector[s] further comprises a nucleic acid encoding an immunostimulatory [molecule] protein other than an antigen of the infectious disease, autoimmune disease, viral infection, bacterial infection, fungal infection, cancer or foreign peptide fragment against which an immune response is to be induced.

6. (Twice Amended) The method according to claim 1, wherein the second recombinant vector is [comprises] a recombinant vaccinia [virus] viral vector.

7. (Twice Amended) The method according to claim 1, wherein the second recombinant vector is [comprises] a recombinant fowlpox [virus] viral vector.

8. (Twice Amended) The method according to claim 1, wherein the second recombinant vector is [comprises] a recombinant [adenovirus] adenoviral vector.

Claims 9-20 have been canceled.